REMARKS

Claims 6, 7, 9, 10, and 12 are pending in the instant application. Claims 6, 7, 9, 10, and 12 have been rejected. Claims 6 and 10 have been amended. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Rejections Under 35 U.S.C. §112

U.S.C. §112, Second Paragraph

Claims 6-7, 9-10 and 12 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to define the term "rate of proliferation". In an earnest effort to facilitate the prosecution of the instant invention, Applicant has amended claims 6 and 10, and claims dependent therefrom, to indicate that the disclosed fusion protein is used for assessing whether a cell is quiescent or actively growing. Support for this amendment can be found at page 15, line 36, to page 18, line 11. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

U.S.C. §112, First Paragraph, Written Description

Claims 6, 7, 9, 10, and 12 have been rejected for lacking a sufficient description of assessing the rate of proliferation a cell. In particular, the Examiner suggests that the even if "rate of proliferation" were substituted with "growth rate", as disclosed in the specification, the specification fails to provide evidence that the time of degradation of the claimed fusion proteins is related to the proliferation rate of any cell culture. Applicant respectfully disagrees.

Applicant has established that the stability of a UbL domain-containing fusion protein is dependent upon whether a cell is quiescent or actively growing (*i.e.*, logarithmically or exponentially growing). In particular, page 32, lines 10-18, teaches that the half-life of a fusion protein of the instant invention is approximately 1-3 minutes in actively growing cells and greater than 1 hour in quiescent cells. To emphasize this correlation that exists between the stability of an UbL-containing fusion protein and the growth state of a cell, claims 6 and 10 have been appropriately amended. In light of these amendments, reconsideration and withdrawal of this rejection is respectfully requested.

U.S.C. §112, First Paragraph, Enablement

Claims 6-7, 9-10, and 12 have been rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for degradation of $Rad23^{1-369}$, Rad23-HA and Ubl^{R23}-lacZ with 0-30 min. after labeling when the labeling is performed in some exponentially growth yeast transformants (Figures 7 and 9), does not reasonably provide enablement for assessment of rate of proliferation of any cell using any fused DNA encoding a protein consisting of any Ubl domain of SEQ ID NOs:2-12, a linker and a reporter protein. It is acknowledged that the art of construction of DNA molecules encoding fusion proteins is highly developed and skill of the artisan is high; however, it is suggested that because Applicant has not shown any correlation between the rate of proliferation in any cell and kinetics of degradation of the fusion protein, one skilled in the art is forced to perform undue experimentation with low probability of success. It is further

suggested that the degradation of any fusion protein in any multiplying cell was not disclosed and the half-life of any particular construct is dependent upon its structure as evidenced by the teachings of U.S. Patent No. 5,132,213. Applicant respectfully disagrees.

Applicant has demonstrated that the UbL domains of Dsk and yeast and human Rad23 (SEQ ID NO:1-5) fused to reporters such as GST and β-gal bind to the proteasome (see pages 41 and 42), wherein the binding is more favorable in actively growing cells (see page 44, lines 20-22), leading to an decrease in the stability of the fusion protein in actively growing cells with a functional 26S proteasome (see pages 32-33 and the paragraph bridging pages 36 and 37). In an effort to facilitate the prosecution of the instant application, Applicant has amended claims 6 and 10 to clarify the structure of the fusion protein (*i.e.*, having a UbL domain of SEQ ID NO:2-5) and types of cells being assessed (*i.e.*, having a functional 26S proteasome). As Applicant has provided experimental support for the claimed fusion proteins and cell types being assessed, Applicant has satisfied the enablement requirement set forth under 35 U.S.C. §112, first paragraph. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

II. Conclusion

The Applicant believes that the foregoing comprises a full and complete response to the Office Action of record.

Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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